REMARKS

Upon entry of this amendment, claims 1, 3, and 46-57 will be pending in this application. By this amendment, claims 2 and 6 have been cancelled; claims 1, 3, 6, 46, 46, 49-52, 55 and 56 have been amended; and claim 57 has bee added. The amended claims set is provided herewith.

No new matter has been added as a result of the amendments to the claims. The claims have been amended to be more clear or to recite classes of polynucleotides described in the specification.

Written Description Rejection

Claims 1-3, 6 and 46-56 have been rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter that was not described in the specification in such a way as to convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant traverses the rejection to the extent that it is maintained.

The Office Action stated that apart from the specific disclosure of using (i) an exogenous polynucleotide encoding kir/GEM to decrease levels of L-type Ca channels in atrioventricular node cells and thereby decrease the cell excitability; (ii) exogenous polynucleotide encoding a Giα subunit to increase dephosphorylation of the L-type Ca channel and thereby decreasing its conductance; and (iii) a dominant negative Ca(v)1.2 with an ascidian 3-domain type alpha 1 subunit to suppress the expression of L-type Ca channel, the instant specification fails to describe relevant characteristics of a representative number of other species for a broad genuera as claimed.

Independent claim 1 has been amended to recite that the compositions comprise a first polynucleotide encoding (i) a dominant negative N-terminal truncated α1 subunit of an L-type Ca^{2+} channel[1] or (ii) kir/GEM and a second polynucleotide encoding a $G_{i\alpha}$ subunit. Independent claim 51 has been amended to recite that the composition comprises a first polynucleotide

[1] It can be inferred from paragraph 73 of the present published application that the ascidian 3-domain-type alpha 1 subunit lacks an N-terminus from the title of the cited FEBS article. On reading the article, one would be readily able to verify this inference.

encoding kir/GEM and a second polynucleotide encoding a $G_{i\alpha}$ subunit. According to the Office Action, such polynucleotides are adequately described in the specification.

In light of the amendments to independent claims 1 and 51, withdrawal of the rejection is respectfully requested.

Indefiniteness Rejection

Claims 1-3, 6 and 46-56 have been rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. Applicants traverse the rejection to the extent it is maintained.

The Office Action stated that the term "substantially extinguish" is a relative term rendering the claim indefinite. Without acquiescing to the logic presented in the Office Action, applicant asserts that the claims as amended no longer recite "substantially". Accordingly, withdrawal of the rejection is respectfully requested.

§ 103 Rejection of the Claims

Claims 1-3, 6 and 46-56 have been rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Donahue et al, U.S. 2002/0155101 in view of Murata et al. (Circulation 106:19, abstract 36, 2002). Applicant respectfully traverses the rejection to the extent it is maintained.

The Office Action stated that Donahue et al. disclose a composition comprising one or more polynucleotides that encode the inhibitory Gαi2 subunit, G-protein subunit, connexin, gap junction protein and at least one ion channel protein including L-type Ca channel subunits having dominant negative activity and others including genes for proteins affecting arrhythmias to cause a decrease in the speed of conduction through at least the AV node. The Office Action further states that Murata et al. disclose a vector encoding kir/GEM and that the exogenous expression of kir/GEM reduced L-type calcium current and has been previously demonstrated to reduce calcium current in PC12 cells by decreasing expression of L-type Ca channels. In addition, the Office Action stated it would have been obvious for an ordinary skilled artisan to modify the teachings of Donahue et al. by incorporating a vector encoding kir/GEM in their composition to modulate the electrical property of the heart in an experimental model, particularly for decreasing the speed of conduction through at least the AV node, in light of the teachings of Murata et al.

The present claims are directed to bio-ablation compositions having amounts of first and second polynucleotides that when expressed in atrioventricular node cells effectively extinguish conduction through the atrioventricular node. The teachings of Donahue et al. appear to be directed to treating arrhythmias, which as pointed out in the Office Action may include a decrease in the speed of conduction through the AV node (see paragraph 39 of Donahue et al.). For example, Donahue et al. teaches that decreases in conduction of at least about 10%, preferably about 20 to 50% or more are useful. However, such a decrease for treating arrhythmia, does not amount to effectively extinguishing conduction with the bio-ablation compositions of the instant application.

According to the Office Action, Murata et al. disclose a vector encoding kir/GEM and that exogenous expression of kir/GEM reduces L-type calcium channel current. The Office Action further states that it would have been obvious to incorporate a vector encoding kir/GEM into a composition according to Donahue et al. because inactivation of L-type calcium channels via exogenous expression of kir/GEM would serve to decrease conduction through the AV node.

It appears that the Office Action is stating that because Donahue et al. teaches that it is desirable to treat arrhythmias by reducing conduction through the AV node via expression of one or more polynucleotides, it would have been obvious to include a kir/GEM vector that would be expected to reduce conduction as taught by Murata et al. Without acquiescing to the logic presented in the Office Action, Applicant respectfully asserts that even if one were to modify the teachings of Donahue et al. to employ the kir/GEM vector as taught by Murata et al., one would still only arrive at a composition useful for treating arrhythmias rather than a bio-ablation compositions as presently claimed.

That is, bio-ablation compositions configured to effectively extinguishing conduction through the AV node as recited in the present claims would not be useful for treating arrhythmias as taught by Donahue et al. There is nothing in the combined teachings of Donahue et al. and Murata et al. that would lead one to formulate a composition that would effectively extinguish conduction through the AV node. As such, the combined teachings of Donahue et al. and Murata et al. do not render obvious the compositions of the claims presently pending in the instant application.

Withdrawal of the rejection is respectfully requested.

Conclusion

In view of the foregoing amendments, Applicants respectfully request reconsideration and allowance of the claims as all rejections have been overcome. Early notice of allowability is kindly requested. The Examiner is respectfully requested to contact the undersigned by telephone at 763.514. 4673 or by E-mail at carol.f.barry@medtronic.com with any questions or comments. Please grant any extension of time, if necessary for entry of this paper, and charge any fee due for such extension or any other fee required in connection with this paper to Deposit Account No. 13-2546.

Respectfully submitted,

August 7, 2007
Date

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